Industry-related Outbreak of Human Anthrax

To the Editor: In his letter, Industry-related Outbreak of Human Anthrax, Massachusetts, 1868 (1), Dr. Macher suggests an additional reference to cases of industry-related anthrax that occurred in the United States in the 1800s. Our paper exclusively addressed bioterrorism-related inhalational anthrax (2). In our introductory paragraph we referred to woolsorter's disease and ragpicker's disease, terms used to describe textile industry–related inhalational anthrax rather than cutaneous disease (3,4). The citation to which Dr. Macher refers describes eight patients that had cutaneous lesions consistent with cutaneous anthrax; some also had evidence of secondary bacteremic dissemination (5). Dr. Macher suggests that the symptoms of chest distress, chest pain, dyspnea, and tachypnea described in some of the patients are evidence of "mediastinal involvement." However, these symptoms may be consistent with bacteremic dissemination of *Bacillus anthracis,* and their presence is not sufficient evidence to conclude that these patients had hemorrhagic mediastinal lymphadenopathy, the pathologic hallmark of inhalational anthrax. In addition, the observed case-fatality rate of 25% in these patients is consistent with untreated cutaneous anthrax and contrasts sharply with the expected case-fatality rate of >85% for untreated inhalational disease (4,6).

John A. Jernigan,*
David S. Stephens,*
David A. Ashford,*
and Bradley A. Perkins*

*Centers for Disease Control and Prevention, Atlanta, Georgia, USA

References

1. Macher A. Industry-related outbreak of human anthrax: Massachusetts, 1868. Emerg Infect Dis 2002;8:1182.
2. Jernigan J, Stephens D, Ashford D, et al. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. Emerg Infect Dis 2001;7:933–44.
3. LaForce F. Woolsorter's disease in England. Bull N Y Acad Med 1978;54: 956–63.
4. Brachman P. Inhalation anthrax. Ann N Y Acad Sci 1980;353:83–93.
5. Stone S. Cases of malignant pustule. Boston Med Surg J 1868;I (N.S.):19–21.
6. Dixon T, Meselson M, Guillemin J, Hanna P. Anthrax. N Engl J Med 1999;341: 815–26.

Address for correspondence: John Jernigan, Centers for Disease Control and Prevention, 1600 Clifton Rd., MS E68, Atlanta, GA 30338, USA; fax: 404-498-1244; email: jqj9@cdc.gov

In Reply: Jernigan et al. state that they exclusively addressed cases of inhalational anthrax in their 2001 report. However, I question whether their patient 8, a mail sorter with a "healing scab on the anterior neck," can be classically characterized as a pure case of inhalational anthrax.

On October 14, 2001, a 56-year-old female mail sorter (patient 8) in New Jersey became ill with vomiting and diarrhea, followed the next day by chills and fever. The vomiting and diarrhea improved, but during the next 2 days, she had shaking chills, fever, headache, and fatigue. A nonproductve cough developed, along with mild shortness of breath and anterior chest pain on inspiration. On October 19, with persistent fever and worsening chest pain, she went to a local emergency room. She appeared ill with increased respiratory effort and had a 0.5- to 1.0-cm healing scab on the anterior neck. A computed tomographic scan of the chest on October 22 demonstrated mediastinal and cervical lymphadenopathy (1).

In 1942, Severn reported a fatal case of pulmonary/meningeal anthrax in a 17-year-old woman whose cutaneous (point-of-entry) lesion had healed (2). The patient had received no specific treatment for anthrax, as such was not even suspected before death; nor had any form of chemotherapy been instituted. Up to 10 days before her illness, the woman had been working in a modern South Wales brush factory. Two days before ending her employment, she had what her parents described as a boil on the middle phalanx of the second finger of the right hand from the center of which her father extracted a bristle that had entered the finger in the course of her work. The lesion subsequently healed without medical aid. Her final illness (high temperature and severe headache) began 12 days after this incident, the patient being quite well in the interval.

An autopsy was performed by Dr. J. Gough, a pathologist at the Cardiff Royal Infirmary. Each pleural cavity contained blood-stained fluid: one half pint on the left side and three quarters pint on the right. The pia-arachnoid was extremely congested over the hemispheres, with subarachnoid hemorrhage on the upper and lateral aspects and along the Sylvian fissures. The brain showed an acute hemorrhagic inflammation of the pia-arachnoid over the hemispheres. The subjacent brain showed an acute inflammation of perivascular distribution in the gray matter. Similar inflammation was present in the basal ganglia and cerebellum. In the lungs, tissues were destroyed in some hemorrhagic areas. From the meninges, brain, spleen, and blood a spore-bearing aerobe was grown in pure culture. The same organism was grown from the lung. The spore-bearing organism was pathogenic for the guinea pig and mouse and identified as *Bacillus anthracis*. The woman had been

employed in sorting horsehair and pig bristle imported mainly from China and South America.

Samples of materials she sorted were tested for bacteria by Dr. V.D. Allison, Ministry of Health, who reported that the seven different batches of suspected horsehair and bristle submitted were heavily contaminated with aerobic spore-bearing organisms, and from one batch of mixed horsehair, he isolated a colony of typical *B. anthracis* that was lethal to a guinea pig.

The clinical history suggests that the portal of entry of the infection was the finger that healed spontaneously, as there was no evidence of this lesion at autopsy (2). I propose that Jernigan et al.'s patient 8 with inhalational anthrax may have also had a cutaneous portal-of-entry infection by the spores of *B. anthracis*.

Jernigan et al. also state that mediastinal involvement does not develop in patients with cutaneous anthrax. In 1918, Gilmour and Campbell (a pathologist) reported the cases of two men who contracted anthrax from shaving brushes contaminated with *B. anthracis*; patient 2 had cutaneous anthrax with mediastinal involvement. He was admitted to Bramshott Military Hospital, Canada, on February 27. On February 22, he had procured a new shaving brush from Quartermaster stores and used it for the first time on February 25; while shaving, he cut his left cheek slightly, causing free bleeding. Toward evening he began to feel poorly; he felt ill during the night. On the morning of February 26, he shaved again and reopened the wound, which again bled freely. Shortly before noon, his face began swelling very rapidly around the cut, down the side of his neck, and in front and behind the ear. During the afternoon he felt worse, had chills, and had a severe headache. He had difficulty swallowing, and the swelling of the neck and face was increasing. During the night, he had great difficulty in swallowing and breathing; he felt as if he were going to choke. He had a severe headache, nausea, vomiting, and chills. On February 27, his temperature was 38.9°C and pulse 140. The left side of his face and neck were very swollen; the swelling extended down over the sternum. Respirations were shallow and impaired. A smear from the malignant pustule on the left cheek demonstrated anthrax bacilli. On February 28, the patient lapsed into a coma and died. A postmortem examination showed that "mediastinal tissues were extremely edematous" (3).

Note the similarities between Gilmour and Campbell's patient 2 and Stone's patient 5, a laborer at a Massachusetts' animal hair factory (4). Patient 5 contacted Dr. Stone on November 17, 1867. He had been sick since the Thursday previous (14th) and had chills, pain in head and back, and loss of strength. He had previously noticed a pimple on his neck but could not say when it first appeared. The patient primarily had pain and distress in epigastrium and back. The pulse was 120, his breathing was hurried, and his neck was swollen. On November 18, the "slough" (cutaneous lesion) doubled in size, and on November 19, a severe chill developed and edema extended down to the nipple. On November 20, the patient's chest was doughy to the touch as far down as the nipples. On November 21, the patient became delirious, had chest pain, and died that evening. Stone's patient 5 may have also had mediastinal disease (5).

In conclusion, some persons who work in facilities that are contaminated with the spores of *B. anthracis* may experience dual cutaneous and inhalational anthrax infections, and mediastinal disease may develop in some patients with cutaneous anthrax.

Abe Macher*

*Bethesda, Maryland, USA

References

1. Jernigan JA, Stephens DS, Ashford DA, Omenaca C, Topiel MS, Galbraith M, et al. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. Emerg Infect Dis 2001;7:933–44.
2. Severn AGM. Anthrax septicemia—a fatal case. Lancet 1942;1:9–10.
3. Gilmour CH, Campbell AR. Anthrax in man with a report of two cases. Can Med Assoc J 1918;8:97–107.
4. Stone S. Cases of malignant pustule. Boston Med Surg J 1868;I:19–21.
5. Macher A. An industry-related outbreak of human anthrax: Massachusetts, 1868. Emerg Infect Dis 2002;8:1182.

Address for correspondence: Abe Macher; Bethesda, MD, USA; fax: 301-443-8143; email: amacher@hrsa.gov

In Reply: Dr. Macher proposes that the cutaneous lesion on the neck of patient 8 in our series suggests a cutaneous entry. At the time of the patient's initial hospitalization for anthrax, the lesion and its history were evaluated with this possibility in mind. We do not believe the lesion was cutaneous anthrax. The lesion was present before the patient's exposure to *Bacillus anthracis* spores, and its clinical features and course were not compatible with cutaneous anthrax. The presence of mediastinal lymphadenopathy in this patient strongly indicates that the route of exposure was through inhalation.

Dr. Macher refers to case reports of patients with cutaneous anthrax who had evidence of secondary bacteremic dissemination. Patients with bacteremic cutaneous anthrax were also seen in the 2001 outbreak but were not included in our report. The findings in the patients referred to by Dr. Macher included edema, often extensive, of the skin and soft tissues contiguous to the primary cutaneous lesion, as well as edematous changes in multiple other organs and body spaces such as bowel wall, mesentery, omentum, central nervous system,

and peritoneal and pleural spaces (1–3). In one patient in whom the primary lesion was on the face, the postmortem findings included extensive edema of the neck, soft tissues of the chest, and the mediastinum (2). Mediastinal lymphadenopathy was not described in any of these patients. Edema is a well-described feature of *B. anthracis* infection believed to be the result of one of its two binary toxins, edema toxin, which likely causes edema by increasing cellular levels of cyclic AMP and upsetting water homeostasis (4).

Dr. Macher suggests that "mediastinal disease" may develop in cutaneous anthrax patients. We agree that cutaneous anthrax with bacteremic dissemination may result in pathologic changes in multiple organs. Mediastinal edema can result from hematogenous infection of mediastinal tissues, by direct extension from the involved structures of the face and neck, or from systemic effects of circulating toxin. However, edema should not be confused with hemorrhagic mediastinal lymphadenopathy, the classic pathologic change associated with inhalation anthrax. We are unaware of any evidence, including that presented in the case reports referenced to by Dr. Macher, suggesting that hemorrhagic mediastinal lymphadenopathy results from cutaneous anthrax infections. This signature finding in inhalational anthrax is thought to result from phagocytosis of inhaled spores by alveolar macrophages, followed by transportation within phagocytes to the mediastinal lymph nodes where initial multiplication of the bacilli and release of toxin occurs (4).

John A. Jernigan,*
Martin S. Topiel,†
and David S. Stephens*

*National Center for Infectious Diseases Centers for Disease Control and Prevention, Atlanta, Georgia, USA; and †Virtua Health, Mount Holly, New Jersey, USA

References

1. Severn AGM. Anthrax septicemia—a fatal case. Lancet 1942;1:9–10.
2. Gilmour CH, Campbell AR. Anthrax in man with a report of two cases. Can Med Assoc J 1918;8:97–107.
3. Stone S. Cases of malignant pustule. Boston Med Surg J 1868;I:19–21.
4. Dixon TC, Meselson M, Guillemin J, Hanna PC. Anthrax. N Engl J Med 1999;341:815–26.

Address for correspondence: John Jernigan, Centers for Disease Control and Prevention, 1600 Clifton Rd., MS E68, Atlanta, GA 30333; fax: 404-498-1244; email: jqj9@cdc.gov

Correction, Vol. 9, No. 9

On p. 1326, in the article on "Mayaro Virus in Wild Mammals, French Guiana," in the 8th line under "The Study," a serum was incorrectly printed as a dilution. The line should read as follows: Serum samples with titers >20 were confirmed by seroneutralization at a 1:20 dilution (10).

Open Access Publishing Conference

An Open Access Publishing Conference will be held on January 7, 2004 at Emory's Woodruff Health Sciences Center Administration Building Auditorium. The keynote address will be delivered by Dr. Harold Varmus, early advocate of a new model for disseminating scientific research. Other speakers include representatives from the National Library of Medicine, BioMed Central, and the library community. This half-day conference, which is jointly sponsored by CDC Information Center & Emory Health Sciences Center Library, is open to all interested faculty, scientists, public health workers, and librarians. Registration is required. For more information, contact the CDC Information Center at 404-639-1717.

OPPORTUNITIES FOR PEER REVIEWERS

The editors of Emerging Infectious Diseases seek to increase the roster of reviewers for manuscripts submitted by authors all over the world for publication in the journal. If you are interested in reviewing articles on emerging infectious disease topics, please e-mail your name, address, curriculum vitae, and areas of expertise to eideditor@cdc.gov

At Emerging Infectious Diseases, we always request reviewers' consent before sending manuscripts, limit review requests to three or four per year, and allow 2-4 weeks for completion of reviews. We consider reviewers invaluable in the process of selecting and publishing high-quality scientific articles and acknowledge their contributions in the journal once a year.

Even though it brings no financial compensation, participation in the peer-review process is not without rewards. Manuscript review provides scientists at all stages of their career opportunities for professional growth by familiarizing them with research trends and the latest work in the field of infectious diseases and by improving their own skills for presenting scientific information through constructive criticism of those of their peers. To view the spectrum of articles we publish, information for authors, and our extensive style guide, visit the journal web site at www.cdc.gov/eid.

For more information on participating in the peer-review process of Emerging Infectious Diseases, email eideditor@cdc.gov or call the journal office at 404-371-5329.